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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,812	07/10/2001	Diane Pennica	GENENT.083A	7879

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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,812	PENNICA ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,8-10,67-69,71-76 and 78-90* is/are pending in the application.

4a) Of the above claim(s) *84-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-10,67-69,71-76 and 78-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The supplemental amendment filed February 6, 2006, is acknowledged and has been entered. Claims 1, 67, and 74 have been amended. Claims 81-90 have been added.

2. The amendment filed October 6, 2005, is acknowledged and has been entered.

3. Claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-90 are pending in the application and currently under prosecution. Claims 84-90 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-83 are currently under prosecution.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

6. Newly submitted claims 84-90 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-83 have been examined to the extent that those claims read on the elected invention, which is the invention of Groups 44 and 45 (after rejoinder of claims directed to the invention of Group 44), originally claims 1-10, drawn to a method for the selective enhancement of the expression of Stra6 in a colon cancer or breast cancer cell comprising treating the cell with a retinoid.

In contrast, the elected invention, newly added claims 84-90 are directed to a method comprising identifying a tumor cell characterized by aberrant signaling of a member of the Wnt pathway and treating the tumor cell with an effective amount of a retinoid to selectively enhance expression of a Stra6 protein.

Accordingly, the inventions of claims 84-90 do not necessarily share the same purpose or objective as the claims directed to the elected invention, namely the selective enhancement of the expression of Stra6 in a colon cancer or breast cancer cell. Furthermore, the processes of claims 84-90 are materially different processes comprising different process steps, since those processes comprise first identifying a tumor cell characterized by aberrant signaling of a member of the Wnt pathway and then treating the identified tumor cell with an effective amount of a retinoid to selectively enhance expression of a Stra6 protein.

Because of these differences, the inventions of claims 84-90 are patentably distinct from the elected invention.

Because the inventions of claims 84-90 and the elected invention are patentably distinct for these reasons, the search necessary to consider the merit of the newly added claims is not the same, nor is it coextensive with the search that has been necessary to consider the merit of claims directed to the elected invention. Consequently, consideration of the newly added claims would require the performance of a new and different search, which would be unduly burdensome.

Therefore, it is proper to restrict the inventions of claims 84-90 from the elected invention. See MPEP § 803.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 84-90 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Grounds of Objection and Rejection Withdrawn

7. Unless specifically reiterated below, Applicant's amendment and/or arguments submitted October 6, 2005, or February 6, 2006, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed June 6, 2005.

Grounds of Rejection Maintained

Claim Rejections – 35 USC § 112

8. The rejection of claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-83 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is maintained.

At pages 6-10 of the amendment filed October 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

At pages 6 and 7 of the amendment, Applicant has argued that the adequate description of every tumor cell characterized by aberrant Wnt signaling is not a requirement set forth under 35 U.S.C. § 112, first paragraph.

In reply, the written description provision set forth under § 112, first paragraph, requires the claimed subject matter be described with the particularity necessary to permit the skilled artisan to immediately envision, recognize, or distinguish that subject matter, as otherwise the disclosure would not reasonably convey that Applicant had possession of the claimed invention at the time the application was filed.

Beginning at page 7 of the amendment, Applicant has argued the disclosure is adequate to show Applicant's possession of the claimed invention at the time the application was filed. To the contrary, however, as stated in each of the preceding Office actions, the disclosure would not permit the skilled artisan to immediately

envision, recognize, or distinguish at least a substantial number of tumor cells characterized by aberrant Wnt signaling, or to reasonably convey to the skilled artisan that Applicant had possession of the genus of tumor cells, and the claimed invention, at the time the application was filed. Again, the specification defines the term "characterized by aberrant Wnt signaling" as including "genetic defects and/or altered expression patterns (including mutations, amplification, over-expression and/or suppression) of any of these members of the Wnt signaling pathway, or any other members, known today **or hereinafter identified**" (emphasis added) (lines 9-11). As such, the claims are directed to a member of a genus of tumor cells that are characterized as having genetic defects and/or altered expression patterns, including mutations, amplification, over-expression, and/or suppression of any member of a genus of known, *or yet to be discovered* proteins involved in a Wnt signaling pathway. While those members of the Wnt signaling pathway, which have yet to be discovered, cannot have been adequately characterized to permit the skilled artisan to immediately recognize or distinguish those genes or their products from any others, it is noteworthy that even the disclosed or known members of the genus have such substantially disparate structures and functions that there does not appear to be any particularly identifying structural and/or functional features that are shared by those members, which set recognizably or distinctively set apart those gene and their products from any other.

Again, the Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568). In this instance, because the specification specifically directs the artisan to the use of tumor cells harboring defects causing aberrant expression of any hereinafter identified members of a Wnt signaling pathway, the disclosure cannot be reasonably said to have adequately described the genus. Moreover, because of the unpredictable nature of the art, the disclosure of the few known members of the pathway cannot be

reasonably said to be representative of the genus, as a whole, especially since those known members appear to have no common distinguishing structural or functional features.

Again, "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes the genus of genes and proteins involved in a Wnt signaling pathway, there is no language that adequately describes the genus of tumor cells that are characterized by aberrant Wnt signaling, and there is no language that adequately describes the genus of tumor cells that are treated with an effective amount of a retinoid to achieve the claimed effect.

Again, "[r]egardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding tumor cells that are characterized by aberrant Wnt signaling, which when treated with a retinoid, selectively express a Stra6 protein at enhanced levels; without such tumor cells, it is impossible to practice the invention. A claimed invention that cannot be practiced because of the insufficiency of the disclosure to adequately describe the invention in a manner that would permit the skilled artisan to know or readily determine infringing subject matter cannot be an invention that has been described with the requisite degree of particularity necessary to convey Applicant's possession of the invention at the time the application was filed.

Again, although the skilled artisan could potentially identify such tumor cells that might be used in practicing the claimed invention by performing experiments that are designed to identify members of a Wnt signaling pathway and detect tumor cells having defects or abnormalities in a Wnt signaling pathway that result from mutations affecting the expression or activity of those members, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate

written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

It is therefore not convincingly argued, as Applicant has done at pages 7 and 8 of the amendment, the disclosure would be sufficient to enable the skilled artisan to identify such tumor cells that might be used in practicing the claimed invention by performing experiments that are designed to identify members of a Wnt signaling pathway and detect tumor cells having defects or abnormalities in a Wnt signaling pathway that result from mutations affecting the expression or activity of those members.

Beginning at page 8 of the amendment, Applicant has noted certain claims are specifically directed to tumor cells characterized by aberrant Wnt signaling of a member of the Wnt pathway selected from the group consisting of Wnt gene family, APC, catenin, frizzled receptors, disheveled protein, glycogen synthetase kinase-3β, transcription factor TCF/LEF-1, nodal related 3 gene, Xnr3, the homeobox genes, engrailed, goosecoid, twin, (Xtwin), siamosis, c-myc, and the WISP genes. In response, while such claims are indeed more specifically directed to certain "subspecies" of the larger genus of tumor cells characterized by aberrant Wnt signaling (e.g., tumor cells characterized by aberrant Wnt signaling of a "homeobox gene", the claimed subject matter has still not been described with the requisite degree of particularity to reasonably convey to the skilled artisan that Applicant had possession of this claimed invention at the time the application was filed.

As noted in the preceding Office action, the claims have been amended to recite, "for the enhancement of the expression of **a Stra6 protein**" (emphasis added), whereas claim 5 (now canceled), which had been considered in the prior Office actions, limited the protein of claim 1 to Stra6, as opposed to "a Stra6 protein". While Stra6 is a known protein, the claims are now more broadly directed to a genus of "Stra6" proteins, including but not limited to Stra6. Now, as Applicant has noted at page 8, the claims are now more specifically directed to a genus of "Stra6" polypeptides, which have at least 95% identity to a polypeptide comprising an amino acid sequence of SEQ ID NO: 2. Because "an amino acid sequence" of SEQ ID NO: 2 is two or more contiguous amino acids of that sequence, the claims are directed to a genus of "Stra6" polypeptides, which have at least 95% identity to any polypeptide having two or more contiguous amino acids of the amino acid sequence of SEQ ID NO: 2. Accordingly, the claims are directed to a genus of polypeptides that differ substantially both in terms of their structures, as well as their functions. Considering this fact, the polypeptide of SEQ ID NO: 2 is not reasonably deemed representative of the genus, as a whole. Consequently, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the genus of polypeptides to which the claims are now directed. For this reason, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). "Guidelines" further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an

adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

Applicant has again argued that given the present knowledge in the art regarding the Wnt signaling pathway, the instant description of multiple species of tumors cells characterized by aberrant Wnt signaling would reasonably convey that Applicant had possession of the claimed invention at the time the application was filed. However, as explained previously, since the members of the genus are so variant in structure and function, the instant description of some species of tumor cells characterized by aberrant Wnt signaling cannot suffice to describe the genus as a whole, because, even given benefit of the instant disclosure of the claimed invention, the skilled artisan could not instantly envision, recognize, or distinguish at least a substantial number of the members of the genus. The examples described are not representative of the genus as a whole, since, for example, the genus includes members characterized by defects or abnormal levels of expression of signaling molecules, which have yet to be discovered, isolated, or described.

Furthermore, apart from the tumor cells described in the specification as having aberrant Wnt signaling, the skilled artisan cannot envision or predict the nature of the genetic defects and/or altered expression patterns, including mutations, amplification, over-expression, and/or suppression of the known members of the Wnt signaling

pathway, so as to immediately recognize any other tumor cells having aberrant Wnt signaling.

Applicant has again argued that given the description of the members of Wnt signaling pathways provided and the further description of multiple examples of tumor cells or tissues that have been found to have altered expression of such members, the specification would permit the skilled artisan to recognize the tumor cells necessary to use the claimed invention. As also previously explained, the members of Wnt signaling pathways that are adequately described in the specification are not representative of the members that have not been described, as the skilled artisan could not immediately envision, recognize or distinguish such other members of the genus; therefore, the skilled artisan could not immediately envision, recognize or distinguish at least a substantial number of the tumor cells to which the claims are directed. Furthermore, given the breadth of the claims, or more particularly the size and variability of the genus of proteins involved in a Wnt signaling pathway, the examples of tumor cells that are provided in the specification cannot be reasonably be considered representative of the genus of tumor cells characterized by aberrant Wnt signaling.

For all of the above reasons, although Applicant's arguments have been carefully considered, none have been found persuasive or sufficient to overcome this ground of rejection of the claims, as failing to satisfy the written description requirement set forth under 35 U.S.C. § 112, first paragraph.

Claim Rejections - 35 USC § 102

9. The rejection of claims 1, 3, 4, 8-10, 67-69, 71-76, 78-80, and 82 under 35 U.S.C. 102(a) as being anticipated by Chu et al. (of record), as evidenced by Pennica et al. (of record) and Szeto et al. (of record), is maintained.

At pages 10-13 of the amendment filed October 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling with an amount of a retinoid effective to selectively enhance the expression of a Stra6 protein in those cells. The prior art teaches treating such tumor cells with a retinoid. Although the prior art does not expressly teach that those tumor cells treated with the retinoid are characterized by aberrant Wnt signaling, as evidenced by Pennica et al., HT-29 colon cancer cells are characterized by aberrant Wnt signaling, since Pennica et al. discloses the gene encoding WISP-1 is amplified in those cells (page 14720, column 2). While the prior art does not teach that the amount of the retinoid used to treat the tumor cells was an amount effective to enhance the expression of a Stra6 protein in those tumor cells, because the prior art teaches treating the tumor cells with retinoic acid induces gene expression in those cells, the amount of the retinoid is in fact capable of selectively enhancing the expression of genes in the cells; more particularly, the amount of retinoid is reasonable deemed an amount effective to enhance the expression of *any* gene that is induced by such treatment. As evidenced by Szeto et al., the gene encoding Stra6 is retinoic acid-responsive; and therefore, it is reasonably expected that the process disclosed by the prior art did in effect cause the selective enhancement of expression of a Stra6 protein in the tumor cells treated with the retinoid.

As noted previously, however, the Office does not have the facilities for examining and comparing Applicant's process with the process of the prior art. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed process and the process taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

Otherwise, Applicant has notably reiterated several arguments; these arguments have been carefully considered but not found persuasive for the reasons set forth in the preceding Office actions.

10. The rejection of claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-82 under 35 U.S.C. 102(b) as being anticipated by van der Leede et al. (*Mol Carcinog.* 1993; 8 (2): 112-122), as evidenced by Szeto et al. (of record), is maintained.

At pages 13 and 14 of the amendment filed October 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling with an effective amount of a retinoid to enhance the expression of a Stra6 protein in those cells. van der Leede et al. teaches treating colon carcinoma HTC116 cells with retinoic acid; see entire document (e.g., the abstract). Although van der Leede et al. does not expressly teach that HTC116 cells are characterized by aberrant Wnt signaling, or that treating these tumor cells with retinoic acid selectively induces the expression of Stra6 in those cells, as evidenced by Szeto et al., HCT116 cells carry an activating mutation in the gene encoding β-catenin and treating HCT116 cells with retinoic acid induces the expression of the gene encoding Stra6 in those cells (page 4202, column 2).

11. The rejection of claims 1, 3, 4, 8-10, 67-69, 71-76, and 78-82 under 35 U.S.C. 102(b) as being anticipated by Keogh et al. (*Cancer Biochem Biophys.* 1993 Jun; **13** (3): 209-220), as evidenced by Szeto et al. (of record), is maintained.

At page 14 of the amendment filed October 6, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The claims are drawn to a method comprising treating tumors cells characterized by aberrant Wnt signaling with an effective amount of a retinoid to enhance the expression of a Stra6 protein in those cells. Keogh et al. teaches treating colon carcinoma WiDr cells with retinoic acid; see entire document (e.g., the abstract). Although Keogh et al. does not expressly teach that WiDr cells are characterized by

aberrant Wnt signaling, or that treating tumor cells with retinoic acid selectively induces the expression of Stra6 in those cells, as evidenced by Szeto et al., WiDr cells have lost both copies of the gene encoding APC and treating WiDr cells with retinoic acid induces the expression of the gene encoding Stra6 in those cells (page 4202, column 2).

New Grounds of Rejection

Claim Rejections – 35 USC § 112

12. Claims 67-69 and 71-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

Claims 67-69 and 71-73 recite, "an effective amount of a retinoid to synergistically enhance expression of a Stra6 protein".

At page 6 of the amendment filed October 6, 2005, Applicant has stated support for the amendment of claim 67 and/or the other claims is found throughout the specification, including at page 3, lines 19-27, page 13, line 19, through page 14, line 11, page 9, lines 15-29, page 22, lines 5-15, page 24, line 33, through page 25, line 10, and page 27, line 34, through page 28, line 2.

Contrary to Applicant's assertion, the specification, including the claims, as originally filed, does not provide proper and sufficient written support for the present claim language.

The claims are directed to an amount of a retinoid that is effective to synergistically enhance expression of a Stra6 protein, but the specification, including the claims, as originally filed, does not describe such an amount of any retinoid, which in the absence of Wnt-1 signaling, is effective to synergistically enhance expression of a Stra6 protein enhance expression of a Stra6 protein. For example, at paragraph [0131] of the published application, the specification describes genes, such as Stra6, which are "synergistically upregulated by retinoid treatment and Wnt signaling". However, neither

this disclosure nor any other appears to describe an amount of a retinoid, alone, which is effective to synergistically enhance expression of a Stra6 protein. The "synergistic upregulation" of gene expression is always described in the context of the effect observed when the cells are treated with a retinoid in the presence of effective Wnt signaling, never a retinoid alone and never a retinoid in combination with any other "agent".

In addition, it is aptly noted that at paragraph [0246], for example, of the published application, the term "synergy" is defined simply as the "combined action" of two agents; accordingly, it is apparent that the term "synergistically upregulated", as it appears in claim 67, is intended to mean the combined positive effect of the retinoid and some other unspecified agent upon the expression of the gene encoding the Stra6 protein. Inasmuch as the claims do not specify this other agent is Wnt-1, it appears the claims are directed to a much broader process for upregulating the expression of a Stra6 protein in a tumor cell than that which is otherwise described in the specification.

Regarding newly added claim 81, as well as presently amended claims 74-81, the claims are directed to a genus of proteins termed "catenin". However, the specification, including the claims, as originally filed, describes only β-catenin.

For these reasons, it appears the amendments to the claims have introduced new matter, thereby violating the written description provision set forth under 35 U.S.C. § 112, first paragraph.

These issues might be resolved if Applicant were to point to particular disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary written support for the instant language of the claims.

Conclusion

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
April 17, 2006